Remarks

Further and favorable reconsideration is respectfully requested in view of the foregoing amendment and following remarks.

Thus, claim 37 has been amended to incorporate the subject matter of claim 36. An additional change has been made to correct the spelling of "hydro" to "hydroxy".

Applicant takes the position that these amendments should be entered even though they are presented after a final rejection. The Examiner has already considered the subject matter of claim 36, which as indicated above has been incorporated into claim 37. Therefore, entry of the amendments will not require any further consideration or search of the prior art.

The patentability of the presently claimed invention over the disclosures of the references relied upon by the Examiner in rejecting the claims will be apparent upon consideration of the following remarks.

On page 2 of the Office Action, the Examiner states that claims 10-23 and 37 are rejected under 35 U.S.C. §103(a) as being unpatentable over Majeti (US '554) in further view of Story et al. (US '949). However, in the next sentence, the Examiner states that the rejection is maintained in regards to claims 10-23 and "withdrawn in regards to claim 37." Therefore, Applicants will discuss this rejection as applied only to claims 10-23.

The Examiner, on page 3 of the Office Action, has noted with respect to Story et al. that "Although the reference discloses NSAIDs, the surfactants are used not only for the formation of micelles but also for solubilizing NSAIDs." The Examiner appears to assume that the surfactants according to Story et al. are used for two different purposes: (i) for the formation of micelles, and (ii) for solubilizing NSAIDS. This, however, is not correct since solubilization of the NSAIDs is achieved through micelle formation.

It is stated in column 4, lines 51-55 of Story et al. that the NSAID will be dissolved in the surfactant. Generally, micelles are aggregates of amphiphilic surfactant molecules, in which the hydrophobic regions are oriented to the center of the micelle whereas the hydrophilic regions are exposed to the surface of the micelle, thus being able to make contact with the surrounding

solvent (e.g. water). When surfactants are employed at relatively high concentrations (above the "critical micelle concentration", CMC), micelles may be formed in which drug molecules are incorporated, and are thus "solubilized".

Since Story et al. relates to solubilization of NSAIDs by micelle formation, this teaching cannot be "applied to solubilizing drugs in general", contrary to what the Examiner states on page 3 of the Office Action. Also, nothing in Story et al.'s teaching suggests that this teaching could be applied to "solubilize" any other kind of drug (e.g. the drug substances of Majeti).

Further, solubilization of drugs by micelle formation as taught by Story et al. requires the surfactants to be added at a large excess, relative to the amount of drug (see column 12, Examples 2-11: weight ratio 1:12.4; Example 28: weight ratio 1:23.4). A possible reason for this is that a large number of surfactant molecules is required in order to form a micelle around a single drug molecule.

Due to the specific properties and requirements of micelle formation, the Examiner's statement on page 3 suggesting that "it would have been obvious to use the surfactants and rationale of Story to solubilize the drugs used in the film formulations of Majeti ... the surfactants . . . when used to dissolve active compounds the compounds will be distributed uniformly throughout the film" is incorrect.

First, the active substances taught by Majeti (nicotine, caffeine) can be distributed uniformly throughout the film, since Majeti fails to mention any possible problems relating to uniform distribution (see Examples 1 and 2). Nicotine and caffeine as used by Majeti are sufficiently soluble in water and other solvents, which allows these drugs to be uniformly distributed in a solvent-based composition (see column 3, lines 4-20, and Example 2). Therefore, there was no motivation for using "the surfactants and rationale of Story to solubilize the drugs used in the film formulations of Majeti". Rather, Story et al. are concerned with drugs (NSAIDs) which are generally poorly soluble in water (columns 9-12).

Secondly, when solubilizing drugs by micelle formation as taught by Story et al., excess amounts of surfactants are required in order to allow micelle formation to occur. The skilled person would have been led away from incorporating high proportions of surfactants (more than

10-fold excess) into the compositions described by Majeti (transdermal patch, buccal patch, bioadhesive film, mucoadhesive film) since high amounts of surfactants would be expected to reduce the mechanical strength of the films. Also, surfactants often exert plasticizing effects in polymer-based compositions (e.g. the film compositions described by Majeti).

Therefore, the skilled person would not have considered the possibility of adding micelle-forming concentrations of surfactants into a polymeric film composition as this would be expected to destroy or deteriorate the mechanical properties of the film.

For these reasons, Applicants take the position that the rejection of claims 10-23 based on Majeti in view of Story et al. should be withdrawn.

The rejection of claims 30 and 52 under 35 U.S.C. §103(a) as being unpatentable over Majeti in view of Stanley et al. (US '207) is respectfully traversed.

Initially, Applicants note that claim 30 was previously cancelled. Therefore, this rejection will be discussed only as applied to claim 52.

Claim 52, which is dependent on claim 28, is directed to the use of a nicotine salt, specifically nicotine salicylate, in the composition.

Majeti discloses neither nicotine salts nor hydroxypropylmethyl cellulose (present claim 28), nor a composition comprising a combination of polyvinyl pyrrolidone and hydroxypropylmethyl cellulose as essential components (present claim 28).

Furthermore, Applicants note that present claim 28 relates to a composition which undergoes rapid dissolution or disintegration upon application to the oral cavity. Majeti remains silent as regards the solubility properties of the compositions described in this patent. Example II in column 7 relates to a multilayer buccal dosage form which comprises, inter alia, cellulose acetate butyrate (CAB; also known under the brand name Uvex) which is resistant to water and is water-insoluble.

Further, Majeti fails to teach hydroxypropylmethyl cellulose (HPMC) which in the Examiner's view is interchangeable with hydroxypropylcellulose (HPC). In this connection, the Examiner has referred to Acharya (US 5,686,094) where HPMC and HPC are considered to be equivalents. However, Acharya pertains to water-containing delivery devices (see claim 1),

whereas Majeti's compositions are not water-containing. Therefore, Acharya does not support the notion that HPMC and HPC would represent equivalents when used in Majeti's compositions. Further, Acharya mentions neither nicotine nor nicotine salts. Hence, the prior art would not have recognized HPMC and HPC as equivalents (as alleged by the Examiner) in compositions containing nicotine or nicotine salts.

Majeti's teaching is specifically concerned with compositions containing nicotine base as the active ingredient. As noted above, nicotine base is quite different from nicotine salts as regards certain physical and chemical properties. Therefore, the skilled person would have assumed that the components (e.g. polymers) taught by Majeti were selected so as to be compatible with nicotine base (rather than nicotine in salt form).

Accordingly, Applicants take the position that the rejection of claim 52 based on Majeti in view of Stanley et al. should be withdrawn.

The Examiner states that the rejection of claim 52 under 35 U.S.C. §103(a) based on Majeti in view of Stanley et al. is further applied to claims 24-29, 31, 33-36, 38-40, 53-57 and 61.

With respect to claim 24, Applicants submit that Majeti fails to teach the specific combination of flavoring agents, sweeteners and tartaric acid recited in items iii, iv and v of present claim 24, in a monolayer film containing nicotine salts. While Stanley et al. generally mention flavorings and flavor enhancers, the reference does not teach or suggest the combination of items iii, iv and v of present claim 24.

Furthermore, while it was recognized by Majeti (column 3, lines 4-9) that nicotine has a characteristic odor, this reference fails to indicate which fragrances might be useful for suppressing the unpleasant odor of nicotine. The present invention avoids or alleviates this problem by employing nicotine salts rather than nicotine base, and by combining these nicotine salts with a combination of flavoring agents, sweeteners and flavor enhancing agent as defined in claim 24. Since the specific substances used for this purpose (menthol, mint flavor, aspartame, sorbitol, tartaric acid) were not even mentioned by Majeti, the selection of these components – according to the present invention – cannot be regarded obvious in view of the cited prior art.

With respect to claims 29, 31, 33-36, 38-40, 53-57 and 61, all of these claims are dependent on claim 28, which is patentable over Majeti for the reasons set forth above.

At about the middle of page 5 of the Office Action, the Examiner states that, in regards to claim 57, caffeine may be considered an awakening agent because it has a stimulating effect. However, claim 57 is dependent on claim 10, which is not subject to the rejection in the first paragraph on page 4 of the Office Action.

The rejection of claim 37 under 35 U.S.C. §103(a) as being unpatentable over Majeti in view of Stanley et al. in further view of Story et al. is respectfully traversed.

As indicated above, amended claim 37 now recites that the total concentration of surfactants is in the range of 0.1 to 5%-wt.

In this regard, as also discussed above, Story et al. teaches incorporating excessive amounts of surfactants (relative to the amount of drug incorporated), generally resulting in a total surfactant content which is above 90 %-wt. (see Examples in columns 13-22). Hence, using these surfactants **in a concentration range of 0.1 to 5%-wt.** was not obvious to the skilled person. In addition, none of the three cited documents teaches or suggests the specific combination of surfactants defined in present claim 37.

Since Story et al. teach solubilization of active agents (NSAIDs) only by formation of micelles which requires the use of excess amounts of surfactants, this teaching cannot be applied to Majeti, and the Examiner's statement that "It would have been obvious...to have used the surfactants and mixtures thereof in the compositions of the combined teachings of the primary and secondary references motivated by the desire to ensure the desired pharmaceutical active agent was thoroughly dissolved and made a uniform mixture throughout the film as taught by Story et al." is not correct.

For these reasons, Applicants take the position that the rejection of claim 37 based on these references should be withdrawn.

The rejection of claims 59 and 60 under 35 U.S.C. §103(a) as being unpatentable over Majeti in view of Stanley et al. in further view of Dam (US '574) is respectfully traversed.

Claims 59 and 60 are directly or indirectly dependent on claim 28, which specifies that the film has a thickness of not more than 70 μm. Dam relates to compositions in the form of pastilles, lozenges, gums, gellies (see recipes in the detailed description) which are generally three-dimensional bodies rather than a thin film. Dam mentions the addition of caramel for brown coloring. While there is no doubt that caramel will produce a brown color when admixed to thick compositions, the same would not be expected in the case of thin films having a thickness of not more than 70 μm. Also, according to Dam's teaching, caramel was used only in combination with gelling agents such as gelatin, agar, alginate, etc. Since caramel is a product whose chemical structure is essentially unknown (caramel is produced by heating sugar above its melting point), it was unpredictable whether this substance would be compatible with the specific polymer components recited in present claim 28, polyvinyl pyrrolidone and hydroxypropylmethyl cellulose.

For these reasons, Applicants submit that the rejection of claims 59 and 60 based on these references should be withdrawn.

Therefore, in view of the foregoing amendment and remarks, it is submitted that each of the grounds of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

The Commissioner is authorized to charge any deficiency or to credit any overpayment associated with this communication to Deposit Account No. 23-0975, with the EXCEPTION of deficiencies in fees for multiple dependent claims in new applications.

Respectfully submitted,

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